Docket No.: AREX-P02-004
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Madiyalakan *et al.*

Application No.: 09/152,698 Confirmation No.: 4505

Filed: September 2, 1998 Art Unit: 1642

For: THERAPEUTIC COMPOSITIONS THAT PRODUCE AN IMMUNE RESPONSE Examiner: K. A. Canella

DECLARATION UNDER 37 C.F.R. § 1.132

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Birgit C. Schultes, Ph.D., of 12 Monadnock Road, Arlington, MA, hereby declare and state as follows:

1. I am Senior Director of Research at Unither Pharmaceuticals, and an inventor on the present application. I have been conducting research in the field of tumor immunology for approximately 16 years. A copy of my *curriculum vitae* is enclosed with this Declaration.

2. I have read the Office Action issued by the U.S. Patent and Trademark Office on February 9, 2005 in the above-identified patent application. I have also reviewed the references cited in the Office Action, including:

- Kedar et al., *Advances in Cancer Research*, 1992, 59:245-323 ("*Kedar*"),
- Crowley et al., *J. Exp. Med.*, 1990, 172:383-386 ("*Crowley*"),

- International Publication No. WO93/20185 by Steinman ("*Steinman*"),
- Sallusto et al., *J. Exp. Med.*, 1994, 179:1109-1118 ("*Sallusto*"),
- De La Salle et al., "FcγR on Human Dendritic Cells" In Human IgG Receptors (textbook), 1996, pages 39-55 ("*De La Salle*"),
- Schwartz, Cancer : Principles and Practice of Oncology (4th Ed.) vol. 1, pages 531-542 ("*Schwartz*"),
- Vrba et al., *PNAS*, 1975, 72 :4602-4606 ("*Vrba*"),
- Paul, Fundamental Immunology (textbook), 1993, p. 1163 ("*Paul*"),
- Jurncic-Winkler et al., *Eur. Urol.*, 1993, 24:487-491 (abstract) ("*Jurncic-Winkler*"),
- Simitsek et al., *J. Exp. Med.*, 1995, 181:1957-1963 ("*Simitsek*"),
- Dong et al., "Vaccine Design: The Subunit Approach" (textbook), 1995, pp. 625-643 ("*Dong*"),
- U.S. Patent No. 5,976,818 to O'Brien et al. ("*O'Brien*"), and
- Baum et al., *Cancer Research*, 1994, 73(3):1121-1125 ("*Baum*").

I have also reviewed the pending claims and the specification of the present application.

3. I understand that the Examiner has stated that based on the teachings of the above cited references, at the time the invention was made, one of ordinary skill in the art would have been motivated to stimulate an immune response against more than one epitope of a tumor associated antigen by administering to a patient having a tumor a soluble complex of a tumor associated antigen and an antibody or antigen binding fragment thereof. However, for the reasons discussed below, a person of ordinary skill in the art, at the time the invention was made, would not have been motivated to combine the teachings of the cited references to reach the invention recited in the pending claims. Furthermore, for the reasons discussed below, even if the references were combined a person of ordinary skill in the art would not have reasonably expected that the administration of a tumor antigen/antibody complex would break the immune tolerance that is often associated with tumor antigens, and elicit a multi-epitopic immune response against the tumor antigen. The references cited below taught that prior to the time the invention was made it was

very difficult to induce an immune response against a tumor antigen because the hosts have various mechanisms or pathways to limit their immune responses against self antigens.

4. The ten references cited by the Examiner can be divided into two groups: one relating to tumor antigens (tumor immunology) and another one relating to foreign antigens.

5. As discussed in detail below, at the time the invention was made, it was well recognized that tumor antigens and foreign antigens were processed and/or presented differently by the immune system. Foreign antigens generally elicit a strong immune response; while tumor antigens generally do not.

6. At the time the invention was made, the art was still searching for effective ways of inducing immune responses against tumor antigens, a much bigger challenge than inducing immune responses to foreign antigens. A major obstacle in using tumor antigens to elicit an immune response is that the host is generally tolerant to tumor antigens. Tumors arise from self, and express self antigens. As summarized in *Paul*, a textbook cited by the Examiner, tumor antigens often have various mechanisms for escaping or failing to elicit an immune response. For example, there are pathways for the deletion of auto-reactive B cells, associated antibodies and auto-reactive T cells. In addition, tumor cells can release factors that could inhibit or kill T cells directly. At the time that the invention was made, the tolerance against self antigens was a well-recognized obstacle for the development of effective immune responses against tumor antigens. *See, e.g.,* Sotomayor et al., "Tolerance and Cancer: A Critical Issue in Tumor Immunology," *Crit. Rev. Oncog.* 7(5-6):433-456 (1996) (Exhibit A) emphasizing that a better identification and understanding of the factors involved in tumor-induced tolerance is required for the development of novel cancer immunotherapies. A review article published two years after the earliest filing date of the present application, Antonia et al., "Immunologic nonresponsiveness to tumors," *Crit. Rev. Oncog.* 1998;9(1):35-41 (Exhibit B) ("*Antonia*"), notes that T cells are generally not effective in rejecting tumors and that T cells are often tolerant to tumor antigens. *Antonia* further states that "tumor cells can acquire attributes that interfere with an immune response including down-regulation of MHC molecules or other

molecules involved in antigen processing." These references demonstrate that, at the time the invention was made, the art had not found a safe and effective way to break the tolerance that is generally associated with tumor antigens.

7. In contrast, immune responses to foreign antigens are readily induced when a foreign antigen is presented by professional antigen-presenting cells (APCs). Factors released by bacteria, viruses, fungi or parasites, including lipopolysaccharides, viral or bacterial DNA and RNA, and many other factors that bind TOLL receptors on the APC, upregulate or activate T and B cells (either directly or indirectly by upregulating other co-stimulatory factors or upregulating secretion of cytokines). Tumors or tumor antigens do not secrete such factors which upregulate or activate immune responses.

8. As discussed above, at the time the invention was made, it was recognized that the processing of foreign and tumor antigens, and the mechanism by which foreign and tumor antigens elicit an immune response, were different. For this reason, a person of ordinary skill in the art would not have been motivated to combine the teachings of references relating to foreign antigens with the teachings of references relating to tumor antigens.

9. *Crowley, Sallusto, De la Salle* and *Simitsek* are references relating to foreign antigens. These references do not relate to tumor recognition or tolerance to tumor antigens. None of these references disclose or suggest the use of tumor antigen/antibody complexes to break the immune tolerance that is often associated with tumor antigens, and induce an effective immune response to a tumor antigen. Moreover, one of ordinary skill in the art at the time the invention was made would not have considered the teachings of these references to be relevant to the issue of breaking the immune tolerance associated with tumor antigens.

10. *Kedar, Schwartz, Jurncic-Winkler, Vrba* and *Steinman* are the only references cited by the Examiner relating to tumor antigens. *Kedar* teaches the use of cocktails of antibodies or T cell clones to treat cancer. *Schwartz* teaches that tumor markers can be shed into the serum. *Jurncic-*

Winkler and *Vrba* teach that tumor antigens can be multi-epitopic. *Steinman* teaches that dendritic cells can present tumor antigens onto class I MHC molecules. None of these references teach the administration of antibody/tumor antigen complexes to induce an immune response to a tumor antigen, and to break the tolerance that is often associated with tumor antigens. Further, none of these references teach that a multi-epitopic immune response can be induced to tumor antigens using antigen/antibody complexes.

11. One of ordinary skill in the art, at the time the invention was made, would not have been motivated to combine the teachings of *Kedar*, *Schwartz*, *Jurncic-Winkler, Vrba* and *Steinman* with the teachings of *Crowley, Sallusto, de la Salle* and *Simitsek* because at the time the art recognized that foreign and tumor antigens were processed and/or presented differently by the immune system and did not necessarily elicit the same type of immune responses through the same mechanisms (as evidenced by *Sotomayor*, *Antonia* and *Paul*).

12. Further, at the time of the invention, the art correlated the presence of circulating immune complexes in the serum of cancer patients with a negative prognosis in cancer. See, e.g., Vlock et al., Clinical Correlates of Circulating Immune Complexes and Antibody Reactivity in Squamous Cell Carcinoma of the Head and Neck," *J. Clin. Oncol.* 11(12):2427-2433 (1993) (Exhibit C). In view of this information, a person of skill in the art would be discouraged from using immune complexes formed from a soluble tumor antigen and an antibody (or antigen binding fragment thereof) to break the immune tolerance that is generally associated with tumor antigens.

13. Moreover, even if the references were combined, at the time that the invention was made, a person of ordinary skill in the art would not have reasonably expected that the administration of a tumor antigen/antibody complex would break the immune tolerance that is often associated with tumor antigens, and elicit a multi-epitopic immune response against the tumor antigen. None of the cited references (whether taken independently or combined with each other) suggest or provide any evidence that a tumor antigen/antibody complex could be immunogenic and break the immune tolerance that is generally associated with tumor antigens. Instead, the cited references prior to the

time the invention was made taught that it was very difficult to induce an immune response against a tumor antigen because the hosts have various mechanisms or pathways to limit their immune responses against self antigens..

14. I further state that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: Aug. 4, 2005

Signed: B. Schultes

Dr. Birgit C. Schultes

BIRGIT C. SCHULTES, Ph.D.

12 Monadnock Rd.
Arlington, MA 02476
USA
Phone: (781) 648-4368

E-mail: bsch.bsch@verizon.net

Unither Pharmaceuticals, Inc.
15 Walnut Street, Suite 300
Wellesley, MA 02481
USA
Phone: (781) 416-1551
Fax: (781) 235-7241
E-mail: bschultes@unither.com

EMPLOYMENT HISTORY

2004-present	**Senior Director**, Research Unither Pharmaceuticals, Inc., Wellesley, MA, USA
2002-2004	**Vice President**, Research AltaRex Corp., Waltham, MA, USA
2000-2002	**Director,** Research and Clinical Immunology AltaRex Corp., Waltham, MA, USA
1998-2000	**Director,** Preclinical Research AltaRex Corp., Edmonton, AB, Canada
1996-1998	**Scientist and Senior Scientist**, Research & Development AltaRex Corp., Edmonton, AB, Canada
1995-1996	**Scientist**, Research & Development Biomira Inc., Edmonton, AB, Canada
1994-1995	**Postdoctoral Fellow**, Research & Development Biomira Inc., Edmonton, AB, Canada
1990-1993	**Supervisor**, Clinical Chemistry, Tumor Marker Laboratory Clinic of Nuclear Medicine, University of Bonn, Germany

EDUCATION

1989-1993	Ph.D., summa cum laude, Cell Biology/Immunology University of Bonn, Germany
1982-1989	M.Sc., Biology (Genetics, Cell Biology, Biochemistry) University of Bonn, Germany and University of Cologne, Germany, Thesis on purification and characterization of an enzyme that regulates DNA metabolism.

MEMBERSHIP OF SCIENTIFIC SOCIETIES

American Association for Cancer Research
American Association of Immunologists
American Society of Photobiology
Society of Tumour Targeting

PROFESSIONAL EXPERIENCE

UNITHER PHARMACEUTICALS, WELLESLEY, MA (2004-PRESENT)

Senior Director, Research

Responsible for directing discovery and preclinical research activities related to three antibodies for the treatment of ovarian, prostate and MUC1-expressing cancers. Studies are focussed on the immune enhancing effects of antibodies and on modalities

to counteract immune regulatory networks. My group is responsible for proof-of-concept to preclinical studies in cell-based assays and animal models, mainly outsourced to CRO or in collaboration with academic institutions. Responsible for establishing internal research laboratory operations and obtaining grant funding for activities pertaining to preclinical and translational studies. Other responsibilities include development and validation of clinical immunology assays, management of clinical immune monitoring activities, establishment and coordination of research collaborations with academia and industry, participation in project teams, presentations at scientific meetings, and preparation of preclinical reports, IND submissions and BLA sections.

ALTAREX CORP., EDMONTON, AB, CANADA AND WALTHAM, MA (1996 TO 2004)

VP, Research and Director, Research and Clinical Immunology (2001 to 2004)

Responsible for directing discovery and preclinical research activities related to AltaRex's technology. Studies were focussed on the function of AltaRex antibody products to induce or inhibit immune responses (in particular T cell responses) to cancer antigens, viruses, autoimmune targets and allergens using dendritic cell systems and a variety of functional T cell assays. The lead product, OvaRex® MAb-B43.13, has advanced into Phase III clinical trails; another antibody is in Phase I.

Other responsibilities included project manager for two antibody projects, management of preclinical safety studies, development and validation of bioassays and clinical immunology assay, management of immune monitoring efforts and integration with clinical team, establishment and coordination of research collaborations with academia, presentations at scientific, business development, and fund raising meetings, and preparation of preclinical reports, BLA sections and IND submissions.

Director, Preclinical Research (April 1998 to Dec. 2000)

Responsible for generation and characterization of new antibodies and constructs, biological evaluation of product candidates in animal models and *in vitro* studies, assay development and validation, preclinical testing of drug candidates for toxicology, pharmacodynamics, immunohistochemistry and pharmacokinetics.

Senior Scientist, Research and Development (1997 to March 1998)

Responsible for development of targeted photodynamic therapy. The responsibilities included project management of an immunoliposomal formulation of a photosensitizer to treat solid tumors, coordinating process development and scale-up of hypocrellin (photosensitizer) synthesis, formulation work into antibody-coated liposomes, assay development, biological evaluation (*in vitro* and *in vivo*) of various hypocrellin formulations and development of animal models. The project was sponsored by a Canadian Government grant.

Scientist, Research and Development (1996-1997)

Responsible for clone development, assay development and *in vitro* characterization of two of AltaRex' s cancer vaccines (for breast and gastro-intestinal cancer).

Responsibilities included supervision of the hybridoma lab in generating new clones for cancer antigens and their characterization for specificity, epitope mapping and affinity, initial evaluation of clones for stability and productivity; testing of their therapeutic activity in various mouse tumor models, supervision of assay development for immunological assays (humoral and cellular) for research and clinical trial support, development, optimization and validation of assays for product development;

pharmacokinetic studies, and characterization of immune responses in animals and patients. Additional responsibilities included writing of SOPs, reports, publications, management of the lab.

BIOMIRA INC., EDMONTON, AB, CANADA (1994-1995)

Scientist, Research and Development (1995)
Responsible for studies on the immunological mechanisms of action of an anti-CA125 antibody for ovarian cancer. Additional responsibilities included antibody *in-vitro* characterization, assay development for immunoreactivity testing of monoclonal antibodies, for clinical immune responses and for serum quantification of the antibody in pharmacokinetic studies in patients, and analysis of serum and lymphocyte samples from clinical trials (PK and immune responses).
Postdoctoral Fellow, Research and Development (1994)
Responsible for studies on the B and T cell activation of immune complexes consisting of an antibody against ovarian cancer and the CA125 tumor-associated antigen *in vitro* and *in vivo*.

UNIVERSITY OF BONN, BONN, GERMANY (1989-1993)
Research Assistant, Clinic for Gynecology and Obstetrics (1989-1993)
Studies on antibody-coupled phthalocyanine for photodynamic therapy
Supervisor, Clinic for Nuclear Medicine (1990-1993)
Responsible for tumor marker laboratory.

PATENTS/PATENT APPLICATIONS

Method and composition for reconforming multi-epitopic antigens to initiate an immune response (Issued), USA 6,241,985

Therapeutic Binding Agents against MUC-1 antigen and methods of their use (Issued), USA 09/641,833

Therapeutic method and composition utilizing antigen-antibody complexation and presentation by dendritic cells (Issued), USA 09/853,300

Reagents and methods for inducing an immune response to prostate specific antigen (Allowed)

Therapeutic compositions that alter the immune response (Pending)

Modulation of the immune system utilizing binding agents targeting immune regulatory receptors (Pending)

Combination Therapy for Treating Diseases (Pending)

Binding agents and their use in targeting tumor cells (Pending)

Therapeutic adjuvant (Pending)

PUBLICATIONS

ORIGINAL ARTICLES IN PEER-REVIEWED JOURNALS (SELECTED ARTICLES FROM OVER 50 PEER-REVIEWED PUBLICATIONS)

T.G. Ehlen, P.J. Hoskins, D. Miller, T.L. Whiteside C.F. Nicodemus, **B.C. Schultes**, K.D. Swenerton. A Pilot Phase II Study of Oregovomab Murine Monoclonal Antibody to CA125 as an Immunotherapeutic Agent for Recurrent Ovarian Cancer. *Int. J. Gynecol. Cancer* 2004 (in press).

J.S. de Bono, S.Y. Rha, J. Stephenson, **B.C. Schultes**, P. Monroe, G.S. Eckhardt, L.A. Hammond, T.L. Whiteside, C.F. Nicodemus, J.M. Cermak, E.K. Rowinsky, A.W. Tolcher. Phase I trial of a murine antibody to MUC1 in patients with metastatic cancer: evidence for the activation of humoral and cellular anti-tumor immunity. *Annals Oncol.* 15:1825-1833, 2004.

J.S. Berek, P.T. Taylor, A. Gordon, M.J. Cunningham, N. Finkler, J. Orr, Jr., S. Rivkin, **B.C. Schultes**, T.L. Whiteside, C.F. Nicodemus. Randomized Placebo-Controlled Study of oregovomab for Consolidation of Clinical Remission in Patients with Advanced Ovarian Cancer. *J. Clin. Oncol.* 22:3507-3516, 2004.

B. C. Schultes, C. N. Nicodemus. Using antibodies in tumour immunotherapy. *Expert Opin. Biol. Ther.* 4, 1265-1284, 2004.

A.N. Gordon, **B.C. Schultes**, H. Gallion, R. Edwards, T.L. Whiteside, J.M. Cermak, C.F. Nicodemus. CA125- and tumor-specific T-cell responses correlate with prolonged survival in oregovomab-treated recurrent ovarian cancer patients. *Gynecol. Oncol.* 94:340-51, 2004..

B.C. Schultes and T.L. Whiteside. Monitoring of Immune Responses to CA125 with an IFN-γ ELISPOT Assay. *J. Immunol. Methods* 279, 1-15, 2003.

V.J. Moebus, R.P. Baum, M. Bolle, R. Kreienberg, A.A. Noujaim, **B.C. Schultes**, C.F. Nicodemus. Immune responses to MAb-B43.13 correlate with prolonged survival of women with recurrent ovarian cancer. *Am. J. Obstet. Gynecol.* 189, 28-36. 2003.

J.S. Berek, **B.C. Schultes**, C.F. Nicodemus. Biologic and immunologic therapies for ovarian cancer. *J. Clin. Oncol.* 21, 168-174, 2003.

J.S. Berek, O. Dorigo, **B. Schultes**, C.F. Nicodemus. Specific Keynote: immunological therapy for ovarian cancer. *Gynecol. Oncol.* 88, S105-109, 2003.

C.F. Nicodemus, **B.C. Schultes**, B.L. Hamilton. Immunomodulation with antibodies: clinical application in ovarian cancer and other malignancies. *Expert Rev. Vaccines* 1, 35-48, 2002.

W. Qi, **B.C. Schultes**, D. Liu, M. Kuzma, W. Decker, A.A. Noujaim, R. Madiyalakan. Characterization of an anti-MUC1 monoclonal antibody with potential for immunotherapy of cancer. *Hybridoma and Hybridomics* 20, 313-323, 2001.

K.A. Berlyn, **B.C. Schultes**, B. Leveugle, A.A. Noujaim, R.B. Alexander, and D.L. Mann. Generation of CD4+ and CD8+ T Lymphocyte Responses by Dendritic Cells Armed with PSA/anti-PSA (antigen:antibody) Complexes. *Clin. Immunol.* 101, 276-283, 2001.

A.A. Noujaim, **B.C. Schultes**, R.P. Baum, R. Madiyalakan. Antibody-Mediated Immunotherapy: Influence of Circulating Antigen on the Induction of Antigen-Specific Anti-Tumor Immune Responses. *Cancer Biotherapy&Radiopharm.*, 16, 187-203, 2001

B.C. Schultes, C. Zhang, L.Y. Xue, A.A. Noujaim, R. Madiyalakan. Immunotherapy of Human Ovarian Carcinoma with OVAREX MAb-B43.13 in a Human-PBL-SCID/BG Mouse Model. *Hybridoma* 18, 47-55, 1999.

B.C. Schultes, R.P. Baum, A. Niesen, A.A. Noujaim, R. Madiyalakan. Anti-Idiotype Induction Therapy: Anti-CA125 Antibodies (Ab3) Mediated Tumor Killing in Patients Treated with Ovarex MAb-B43.13 (Ab1). *Cancer Immunol. Immunother.* 46, 201-212, 1998.

D. Luo, M. Geng, **B. Schultes**, J. Ma, D. Xu, N. Hamza, W. Qi, A.A. Noujaim, R. Madiyalakan. Expression of a Fusion Protein of scFv-Biotin Mimetic Peptide for Immunoassay. *J. Biotech.* 65, 225-228, 1998.

B. C. Schultes, J. Reinsberg, H. Schlebusch, P. Oehr, H.J. Biersack, D. Krebs, and U. Wagner. Idiotypic Cascades in a Mouse Model treated with the Monoclonal Antibody OC125. Induction of Anti-CA 125 Antibodies after Immunization with an Anti-CA 125 (MAb OC125) Antibody by the Activation of the Idiotypic Network. *Eur. J. Clin. Chem. Clin. Biochem.*31: 427-432, 1993.

J. Reinsberg, **B. Schultes**, U. Wagner, D. Krebs. Monitoring of CA 125 in serum of ovarian cancer patients after administration of ^{131}I-F(ab')$_2$ fragments of the OC125 antibody. *J. Clin. Chem.* 39: 891-896, 1993.

U.A. Wagner, P.F. Oehr, J. Reinsberg, S.C. Schmidt, H.W. Schlebusch, **B.C. Schultes**, A. Werner, G. Prietl, D. Krebs. Immunotherapy of Advanced Ovarian Carcinomas by Activation of the Idiotypic Network. *Biotechnology Therapeutics* 3: 81-89, 1992.

B.C. Schultes, E. Fischbach, N. Dahlmann. Purification and characterization of two different thymidine-5'-triphosphate-hydrolyzing enzymes in human serum. *Biol. Chem. Hoppe-Seyler* 373, 237-247, 1992.

S. Schmidt, **B. Schultes**, U. Wagner, P. Oehr, W. Decleer, H. Lubaschowski, H.J. Biersack and D. Krebs. Photodynamic laser therapy of carcinomas - effects of five different photosensitizers in the colony-forming assay. *Arch. Gynecol. Obstet.* 249, 9-14, 1991.

B.C. Schultes and N. Dahlmann. Homogeneous preparation of human thymidine-5'-triphosphatase by electroelution from SDS/PAGE with subsequent renaturation. *Eur. J. Biochem.* 192, 201-205, 1990.

ABSTRACTS, PRESENTATIONS, POSTERS AT SCIENTIFIC MEETINGS (2000 – PRESENT)

B.C. Schultes, H. Eng, K. Agopsowicz, C.F. Nicodemus.
Anti-MUC1 Antibody Enhanced Helper and Cytolytic T Cell Responses with Human Dendritic Cells Presenting MUC1 Antigen or MUC1-Positive Tumor Cells. *Proc. American Association for Cancer Research* 46, 623, 2005; abstract #2649 (oral presentation).

P.T. Taylor Jr., J.S. Berek, **B.C. Schultes**, D.M. Haverstick, C.F. Nicodemus.
Utilization of CA125 Measurements in Oregovomab-Treated Patients. 36th Annual Meeting of the Society for Gynecologic Oncology, March 19-23, 2005, Miami Beach, FL (poster).

B.C. Schultes, H. Eng, K. Agopsowicz, C.F Nicodemus. Potent Helper and Cytoloytic T Cell Responses by Dendritic Cells Armed with MUC1-anti-MUC1 Immune Complexes. 12th International Congress of Immunology & 4th Annual Conference of FOCIS, July 18-23, 2004, Montreal, QC, Canada (poster)

B.C. Schultes, H. Eng, K. Agopsowicz, M. Kuzma, D.L. Mann, T. Whiteside, A.A. Noujaim, C.F. Nicodemus. Antibodies as Vaccines: Immune Complexes Facilitate Tumor Antigen Processing on MHC Class I and II, Induce Dendritic Cell Maturation and Allow for Helper and Cytolytic T Cell Activation. 21st International Conference: Advances in the Application of Monoclonal Antibodies in Clinical Oncology, June 28-30, 2004, Cape Sounio, Greece (oral presentation).

C. F. Nicodemus, P. Taylor, **B. Schultes**, J. Balser, J. S. Berek. Relationship of time to relapse (TTR) and survival post relapse (SPR): exploration of risk factors from the first annual follow-up data set of randomized pbo-controlled study of oregovomab (OV) as a consolidation therapy of patients with advanced ovarian cancer (OC). ASCO, June 5-8, 2004, New Orleans, LA (poster).

J.S. Berek, P. Taylor, A. Gordon, **B. Schultes**, T. Whiteside, C. Nicodemus. First Follow-up to Randomized Study of OvaRex® MAb (OV) for Consolidation of Clinical Remission in Pts with Ovarian Cancer (OC): Prolonged Disease-Free Survival (DFS) in Optimal Chemosensitive Pts. 35th Annual Meeting of the Society for Gynecologic Gynecology, Feb. 7-11, 2004, San Diego, CA (oral presentation).

B. Schultes, A.N. Gordon, C.F. Nicodemus, T.L. Whiteside. Feasibility of combined OvaRex® immunotherapy and chemotherapy in recurrent ovarian cancer. AACR Annual Meeting, July 11-14, 2003, Washington, DC, *Proc. American Association for Cancer Research* 44 (poster).

J.L. Levin, J. Kavanagh, C. Nicodemus, **B. Schultes**, E. Hansen, M. Method. Immunology and pharmacokinetic comparability profiles of OvaRex® (MAb-B43.13) in women with ovarian cancer. AACR Annual Meeting, July 11-14, 2003, Washington, DC, *Proc. American Association for Cancer Research* 44 (poster).

J.S. Berek, P. Taylor, A. Gordon, **B. Schultes**, T. Whiteside, C. Nicodemus. Randomized Pbo-controlled study of OvaRex® MAb (OV) for consolidation of clinical remission in pts with ovarian cancer (OC): prolonged disease-free survival (DFS) in optimal chemosensitive pts. ASCO, May 31 - June 3, 2003, Chicago IL *Proc. ASCO 22* (oral presentation).

B.C. Schultes, M.L. Kuzma, C.C. Zarozinski, K. Agopsowicz, H. Eng. Uptake and processing of antigen-antibody-complexes by human dendritic cells: involvement of multiple receptors and in particular the mannose receptor. AAI Annual Meeting, May 6-10, 2003, Denver, CO (oral presentation).

B.C. Schultes. Antibodies to modulate tumor immunity. Cancer Drug Development, SMi, March 10-11, 2003, London, UK (oral presentation).

H. Eng, M.L. Kuzma, K. Agopsowicz, C.C. Zarozinski, **B.C. Schultes**. Complexation with Murine MAb-B43.13 Alters the Endocytic Trafficking of the Mucinous Tumor Antigen CA125 after Uptake by Human Dendritic Cells. Keystone Symposium "Dendritic Cells: Interfaces with Immunobiology and Medicine", March 3-8, 2003, Keystone, CO (oral presentation).

K. Agopsowicz, M. Kuzma, H. Eng, C.C. Zarozinski, **B.C. Schultes**. Opsonization with specific antibodies enhances dendritic cell presentation of apoptotic tumor cells and induction of CTL. Keystone Symposium "Cell Biology of the Immune Response", March 5-10, 2003, Keystone, CO (oral presentation).

A. Gordon, A. Stringer, H. Gallion, T.L. Whiteside, **B.C. Schultes**, C.F. Nicodemus. Induction of CA125- and tumor-specific IFN-γ T cell responses correlates with prolonged survival in patients

with recurrent epithelial ovarian cancer treated with OvaRex® Mab-B43.13 and chemotherapy. 34th Annual Meeting of the Society for Gynecologic Gynecology, Jan. 31-Feb. 4, 2003, New Orleans, LA (oral presentation).

B.C. Schultes, C.F. Nicodemus, J.S. Berek, T.A. Ehlen, A.N. Gordon, T.L. Whiteside. Use of OvaRex® MAb-B43.13 as an Immunotherapeutic Treatment of Epithelial Ovarian Cancer: Experience as Single Agent post First-Line Therapy and in Combination with Chemotherapy in Recurrent Disease. 14th EORTC-NCI–AACR Symposium on Molecular Targets and Cancer Therapeutics, November 19-22, 2002, Frankfurt, Germany (poster).

H. Eng, M. Kuzma, K. Agopsowicz, C. Zarozinski, **B.C. Schultes**. Opsonization with specific antibodies enhances dendritic cell presentation of apoptotic tumor cells and induction of CTL. 17th Annual Meeting of the Society of Biologic Therapy, Nov. 7-10, 2002, San Diego, CA (poster).

C.F. Nicodemus, **B.C. Schultes**, A.A. Noujaim. Antibody Stimulated Tumor Immunity: OvaRex® MAb-B43.13 in the Treatment of Epithelial Ovarian Cancer. 4th Biennial Ovarian Cancer Research Symposium, Seattle, Sept. 19-20, 2002 (oral presentation).

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